REMARKS

Claims 1, 2, 5, 6, 12, and 13 are currently pending on the merits and under examination. Claims 1 and 6 have been amended to more clearly recite the claimed invention. Claims 7-11, 14, and 17-21 have been withdrawn without prejudice. Claims 3-4 and 15-16 have been canceled without disclaimer or prejudice. Applicants reserve the right to file one or more continuation or divisional applications to any withdrawn or canceled subject matter. No new matter has been added by this amendment.

I. Rejections under 35 U.S.C. § 101 and § 112, First Paragraph, Should be Withdrawn

The rejection of claims 1-6, 12, 13, and 16 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, is maintained on pages 2-5 of the final office action.

Applicants respectfully traverse the rejections. Applicants respectfully submit that the claimed invention does have a specific and substantial asserted utility as disclosed in and supported by the specification for the following reasons.

Applicants submit that the specification discloses that SEQ ID No. 4 is encoded by SEQ ID No. 1. (*See* Specification at page 3, lines 14-15). Therefore, the specification provides support for the cancer related polynucleotide of SEQ ID No. 1 and the encoded polypeptide of SEQ ID No. 4. The specification discloses the detection of SEQ ID No. 6 in PCR cloning, thereby providing support for the nucleotide allele of SEQ ID No. 6.

It appears from the Office Action that SEQ ID Nos. 1, 4 and 6 have been accepted by the Examiner as supported by the specification (*see* January 28, 2009 Office Action at page 4, lines 14-18), but SEQ ID Nos. 2, 3 and 7 are objected to as being not supported by the specification, and no specific comments are provided for SEQ ID No. 8. Applicants respectfully request that the Examiner reconsider the utility and written description rejections of SEQ ID Nos. 2, 3, 7 and 8 in view of the following remarks.

First, please note that SEQ ID Nos. 2 and 3 contain SEQ ID No. 1 and also exist naturally and are over-expressed in liver cancers. As clearly stated in the description, SEQ ID No. 1 is **an intact open reading frame** encoding the protein LAPTM4B-35 (SEQ ID No. 4) without 5' UTR and 3' UTR. SEQ ID Nos. 2 and 3 are **complete cDNAs** with 5' UTR and 3' UTR but with different poly-A tails and different lengths at the 3' end, and particularly, SEQ ID No. 3 is longer than SEQ ID No. 2. (*See* Specification at page 2, line 27 to page 3, line 2). Therefore, both SEQ

ID Nos. 2 and 3 contain SEQ ID No. 1 and are complement to the mRNAs of the LAPTM4B gene. Also, each of SEQ ID Nos. 1-3 encodes the same LAPTM4B-35 protein (*i.e.,* SEQ ID No. 4) and is generally called the LAPTM4B gene (*id.* at page 3, lines 1-2), or more accurately, the cDNAs of LAPTM48 gene or the LAPTM4B*1 allele. (*Id.* at page 13, lines 13-14).

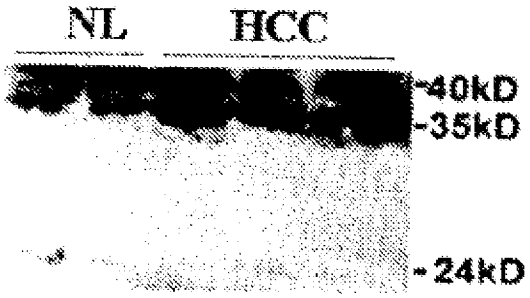
It is also taught in the specification that SEQ ID Nos. 1-3 are present in humans, as they were obtained from human liver tissues via RT-PCR (*see* page 11, lines 17-25 to page 12, lines 2-11) with the primers (*i.e.,* A and E for SEQ ID No. 1). (*See* page 16, lines 16-18 and 24-28). In addition, the expression of LAPFM4B mRNAs in liver cancer tissue and liver cancer cell lines disclosed in the specification was detected by Northern blot (s*ee, e.g.*, Figure 1A and 16; page 3, lines 30-33; page 4, lines 2-4; page 9, lines 13-18 of; and page 11, lines 14-33) and *in situ* hybridization (see Figure 2A; page 3, lines 33-34, page 4, lines 1-2, and page 4, lines 12-16) with a series of probes that are harbored in SEQ ID No. 3, which is the longest one.

Since SEQ ID No. 1 is an ORF sequence but not an intact mRNA molecule, it is not shown in a Northern Blot analysis but is evidenced by Western blot analysis. Although it is not clearly stated in the specification that the Northern Blot analysis (*e.g.,* page 3, lines 30-33) was performed on samples comprising SEQ ID No. 1-3, those skilled in the art could reasonably deduce that samples comprising SEQ ID No. 1-3 were obtained by the same result.

Moreover, SEQ ID Nos. 2 and 3 have been evidenced to be over-expressed in cancer *via* the determination of LAPTM4B mRNA by Northern blot (*see* Figure 1-A and 1-C; page 3, lines 30-33 and page 4, lines 2-4 and 15-16) and *in situ* hybridization (Figure 2-A, page 3, lines 33-34 and page 4, lines 1-2, and page 9, lines 22-24). In addition, the existence and over-expression in cancer of LAPTM4B-35 protein encoded commonly by SEQ ID Nos. 1-3 is firmly evidenced by Western blots with antibody LAPTM4B-17C2,32-241pAb (*see* specification at Figure 3 and page 15, lines 30-33 and page 16, lines 9-10) and by immuno-histochemistry with N1_99pAb. (*Id.* at Figure 11 and page 24, line 13). Therefore, SEQ ID Nos. 1-3 are related to and useful in diagnosis and treatment of cancers.

To summarize, Applicants submit that SEQ ID Nos. 2 and 3 are supported by the description. Indeed, SEQ ID No. 7 is the expression product of SEQ ID No. 6. One of ordinary skill in the art can deduce the amino acid sequence of SEQ ID No. 7 from the nucleotide sequence of the open reading frame in SEQ ID No. 6. As set forth in the specification, the LAPTM4B gene has two alleles, one is *1, SEQ ID Nos. 1-3 and the other is *2, SEQ ID No. 6.

SEQ ID No. 4 is the expression Product of allele *1 and is over-expressed in cancer tissues and cell lines disclosed in the specification, thus it is evidenced that SEQ ID No. 7 would comply with the same as SEQ ID No. 1 based on the expressions of SEQ ID No. 6 in specimens from normal individuals and patients with HCC have been evidenced in the application. (*See* specification at page 21, lines 3-28 and Table 2 and 3). Furthermore, the result of LAPTM4B genotype classification demonstrates the higher occurrence frequency of *2J*2 genotype (*i.e.*, SEQ ID No. 6) in the population with high susceptibility of developing hepatocellular carcinoma. (*Id.* at page 20, lines 24-31). Those of ordinary skill in the art can reasonably deduce the presence of SEQ ID No. 7 in this population. Indeed, the presence in normal liver and up-regulation in liver cancer of SEQ ID No. 7 are also evidenced in the Applicant's studies after the priority date. (*See* below figure).



NL – human normal liver

HCC – human hepatocellular carcinoma

The above figure is an expression profile of LAPTM4B-24, LAPTMB-35, and LAYM4B-40 proteins in human normal livers and liver cancer tissues by Western Blot analysis with anti-LAPTM4B EC2pAb. Page was performed in 12% gel. The LAPTM4B-24, LAPTM4B-35 and LATM4B-40 proteins are all expressed in normal adult livers and hepatocellular carcinoma tissues. LAPTM4B-35 and LATM4B-40 are significantly up-regulated, while LAPTM4B-24 is slightly down-regulated in hepatocellular carcinomas compared .o normal livers. Thus, SEQ ID No. 7 can be used as a target of diagnosis and treatment of the disease as SEQ ID No. 4. Therefore, Applicants submit that SEQ ID No. 7 is supported by the description.

SEQ ID No. 8 is linked continuously with SEQ ID No. 6. SEQ ID No. 8 is a DNA segment comprising the native promoter for the LAPTM4B gene and is linked continuously with

SEQ ID No. 6 and discontinuously with SEQ ID Nos. 1-3. Fig. 17a of the specification shows the relationship between SEQ ID No. 8 (-numbered nucleotide codes in lower case) and the SEQ ID No. 6 (+numbered nucleotide codes in upper case) (*i.e.,* the 3' end of SEQ ID No. 8 from -1341 to -1 is in continuous with the 5' end nt + 1 of SEQ ID No. 6).

In addition, as the promoter of SEQ ID Nos. 1, 2, 3 and 6, SEQ ID No. 8 regulates the transcriptional expression at mRNA level of LAPTM4B gene. (*See* page 7, lines 18-34, page 8, lines 1-12, and Figure 17b). Those of ordinary skill in the art can reasonably deduce that SEQ ID No. 8 comprises the promoter of LAPTM4B gene and can be used as the target of diagnosis and treatment of diseases as the pathogenic gene *per se*. Thus, Applicants submit that SEQ ID No. 8 is supported by the description.

For the reasons discussed above, it is respectfully requested that this rejection of claims 1-6, 13, and 14 under 35 U.S.C. § 101 be reconsidered and withdrawn.

Claims 1-6, 13, and 14 are rejected under 35 U.S.C. § 112, first paragraph, for lacking support of a specific or substantial asserted utility or a well-established utility.

For the reasons discussed above, it is respectfully requested that this rejection of claims 1-6, 13, and 14 under 35 U.S.C. § 112, first paragraph, be withdrawn.

II. Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration and the timely allowance of the pending claims. Should the Examiner find that an interview would be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310.

Respectfully submitted,
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